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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/916,179	Graaf
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 19, 2003*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *20-38* is/are allowed.

6) ☒ Claim(s) *1, 4-14, and 17-19* is/are rejected.

7) ☒ Claim(s) *2, 3, 15, and 16* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claims 1-38 have been amended.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 4-12, 14, and 17-18 are rejected under 35 U.S.C. 103(a) over Reinhard et al. (U.S. Patent 6,432,668 B1) (August 13, 2002) or in the alternative Holmes (U.S. Patent 5,403,717) (April 4, 1995) in view of Arnold et al. (U.S. Patent 6,423,535 B1) (July 23, 2002).

Reinhard et al teach a method of identifying an intestinal polyp comprising the steps of:

a) obtaining a nucleic acid sample derived from intestinal tissue; and

b) determining a gene expression profile from a gene expression product of at least one informative gene having increased expression in an intestinal polyp relative to a control, the gene expression product being a DNA, mRNA, or polypeptide,

wherein increased expression of the gene in the sample is indicative of an intestinal polyp (Column 20, lines 46-67 and Column 2, lines 36-44 and Column 9, lines 49-52).

Reinhard et al inherently teach a method, wherein the gene expression profile is determined utilizing specific hybridization probes and antibodies (Column 20, lines 46-67 and Column 2, lines 36-44 and Column 9, lines 49-52).

Reinhard et al teach a method, wherein one or more informative genes is selected from cell cycle genes (Column 3, lines 5-12).

Holmes teaches a method of identifying an intestinal polyp comprising the steps of:

a) obtaining a nucleic acid sample derived from intestinal tissue; and

b) determining a gene expression profile from a gene expression product of at least one informative gene having increased expression in an intestinal polyp relative to a control, the gene expression product being a DNA, mRNA, or polypeptide,

wherein increased expression of the gene in the sample is indicative of colonic (part of an intestine) polyp (Examples 1-4 and Column 14, line 65 to Column 15, line 19).

Holmes teaches a method, wherein the gene expression profile is determined utilizing specific hybridization probes and antibodies (Examples 11 and 10 respectively).

Holmes teaches a method, wherein one or more informative genes is selected from inflammation genes (Column 14, line 65 to Column 15, line 19).

Reinhard et al. or in the alternative Holmes does not teach a method wherein the gene expression profile is determined utilizing three nucleic acid molecules in oligonucleotide microarrays.

Arnold et al inherently teach a method wherein the gene expression profile is determined utilizing at least three nucleic acid molecules in oligonucleotide microarrays. (Column 7, lines 7-24 and Examples 1 and 3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method wherein the gene expression profile is determined utilizing oligonucleotide microarrays of Arnold et al and one more equivalent genes (two intestinal polyp genes being taught by Reinhard et al. and Holmes) responsible for intestinal polyp in the method of Reinhard et al. or in the alternative Holmes, since Arnold et al. states, "The invention thus provides quantitative information on each element of the microarray. Another advantage of the invention is that the hybridization of the probe sequence and the standard sequences is not competitive, thereby reducing noise in the results (Column 7, lines 19-24)". An ordinary practitioner would have been motivated to combine and substitute a method wherein the gene expression profile is determined utilizing oligonucleotide microarrays of Arnold et al. in the

method of Reinhard et al. or in the alternative Holmes, in order to achieve the express advantages, noted by Arnold et al., of a method that provides quantitative information on each element of the microarray along with another advantage, wherein the hybridization of the probe sequence and the standard sequences is not competitive, thereby reducing noise in the results.

4. Claims 13, and 19 are rejected under 35 U.S.C. 103(a) over Reinhard et al. (U.S. Patent 6,432,668 B1) (August 13, 2002) or in the alternative Holmes (U.S. Patent 5,403,717) (April 4, 1995) in view of Arnold et al. (U.S. Patent 6,423,535 B1) (July 23, 2002) further in view of Lee et al. (Hepatology, (1994), Vol. 19 (3), pages 656-665).

Reinhard et al. or in the alternative Holmes in view of Arnold et al. teaches the claims 1, 4-12, 14, and 17-18 as described above.

Reinhard et al. or in the alternative Holmes in view of Arnold et al. do not teach a method wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1U.

Lee et al. teach a method wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1U (Genbank Accession Number X67493; Abstract, Materials and Methods and Figures 1-2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1U. of Lee et al. in the method of Reinhard et al. or in the alternative Holmes in view of Arnold et al. since Lee et al.

states, "We found that IGFBP-1 gene has several interesting potential regulatory sites and that IGFBP-1 mRNA and protein levels are increased in liver tissue and serum during liver regeneration (Page 657, Column 1, last sentence of third paragraph)". An ordinary practitioner would have been motivated to combine and substitute the method wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1U. of Lee et al. in the method of Reinhard et al. or in the alternative Holmes in view of Arnold et al. in order to achieve the express advantages, noted by Lee et al., of a gene which has several interesting potential regulatory sites and the expression levels of which are increased in liver tissue and serum during liver regeneration.

Allowable Subject Matter

5. Claims 2-3, and 15-16 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 20-38 are allowable.

Response to Amendment

6. In response to amendment, previous 112(first paragraph), double patenting rejections, 102(b), 102(e) rejections and 103(a) rejections are hereby withdrawn. However, new ground of 103(a) rejections based on the same prior art have been provided.

Response to Arguments

7. Applicant's argument to withdraw 102(b) and 102(e) rejections are moot in view of the new 103(a) rejections based on the same prior art.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Arnold et al. since Arnold et al. states, "The invention thus provides quantitative information on each element of the microarray. Another advantage of the invention is that the hybridization of the probe sequence and the standard sequences is not competitive, thereby reducing noise in the results (Column 7, lines 19-24)". This logic is applicable to other 103(a) rejection as well.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 746-4979. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703)605-1237.

Arun Chakrabarti,

Patent Examiner,

March 21, 2003

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